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FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, BIOTECHDS' ENTERED AT 11:41:53 ON
23 OCT 2001
L1 37188 S MEMBRANE AND DISRUP?
L2 13510 S POLYLYSINE
L3 126550 S HISTIDI?
L4 104484 S QUINOLI?
L5 9 S L4 AND L2
L6 9 DUP REM L5 (0 DUPLICATES REMOVED)
L7 30 S L4 AND L1
L8 23 DUP REM L7 (7 DUPLICATES REMOVED)

=> s dna or nucleic or plasmid or polynucleotide
L9 2552716 DNA OR NUCLEIC OR PLASMID OR POLYNUCLEOTIDE

=> s l9 and l8
L10 3 L9 AND L8

=> d bib ab 1-3

L10 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2001 ACS
AN 2000:736711 CAPLUS
DN 134:291165
TI Endogenous neurotoxin selective to dopamine neurons and Parkinson's disease
AU Maruyama, Wakako; Naoi, Makoto
CS Laboratory of Biochemisby and Metabolism, Department of Basic Gerontology, National Institute for Longevity Science, Morioka-cho, Obu, Aichi, 474-8522, Japan
SO Shinkei Kenkyu no Shinpo (2000), 44(4), 527-538
CODEN: SKNSAF; ISSN: 0001-8724
PB Igaku Shoin Ltd.
DT Journal; General Review
LA Japanese
AB A review with 39 refs. The pathogenesis of Parkinson's disease remains to be clarified, and neurotoxins, which occur in the human brain, have been suggested to be involved in it. A dopamine-derived MPTP-like neurotoxin, N-Me (R) salsolinol is one of the most promising candidates of such neurotoxins. The precursor of N-Me (R) salsolinol, (R) salsolinol is enantio-specifically synthesized from dopamine and acetaldehyde by (R) salsolinol synthase. (R) Salsolinol is further N-methylated by neutral (R) salsolinol N-methyltransferase to N-Me (R) salsolinol. N-Me (R)

salsolinol is oxidized non-enzymically and enzymically into 1, 2-dimethyl-6, 7-dihydroxy-iso-quinolinium ion. N-Me (R) salsolinol has been proved to be a neurotoxin selective to dopamine neurons by in vivo and in vitro expts. Continuous injection of N-Me (R) salsolinol in the rat striatum induced behavioral changes, such as akinesia, limb twitching, rigidity of the tail and reduced blinking which reflect dopamine deficiency. Histopathol. observation revealed that dopamine neurons in the substantia nigra were selectively depleted without tissue reaction. To examine N-Me (R) salsolinol is truly involved in the pathogenesis of Parkinson's disease, human materials were analyzed. In the cerebrospinal fluid obtained from parkinsonian patients, the amt. of N-Me (R) salsolinol was significantly higher than that from the patients with multiple system atrophy and normal control. The level of N-Me (R) salsolinol in the cerebrospinal fluid did not correlate with that of homovanillic acid, an indicator of dopamine turnover nor affected by L-DOPA therapy. These results indicate that the level of the neurotoxin was not detd. by dopamine. In the control human brain, N-Me (R) salsolinol was detected in the nigro-striatum and the isoquinolinium ion was detected only in the substantia nigra. The amt. of isoquinolinium ion in the substantia nigra was found to correlate well with the activity of neutral (R) salsolinol N-methyltransferase in the striatum, suggesting that N-methyl-transferase activity is the key factor to det. the level of this neurotoxin in the human brain. The activity of the enzymes related to N-Me (R) salsolinol metab., was examd. using human lymphocytes as an enzyme source. Indeed, the activity of neutral (R) salsolinol N-methyltransferase increased significantly in parkinsonian lymphocytes. The increased activity of neutral (R) salsolinol N-methyltransferase in the lymphocytes and probably in the brain may result in the increase of the neurotoxin level in the brain, and might induce Parkinson's disease after long term of accumulation. The mechanism of the toxicity by N-Me (R) salsolinol was examd. using human dopaminergic neuroblastoma, SH-SY5Y cells. N-Me (R) salsolinol induced apoptosis via disruption of mitochondrial membrane potential and the activation of caspase-3. Structure-activity relationship revealed N-Me (R) salsolinol was much more toxic than another enantiomer, N-Me (S) salsolinol. It indicates that the cells recognize the stereo-chem. structure of N-methyl-salsolinol and that there may be a specific binding site to N-Me (R) salsolinol in the cells. The binding initiates apoptotic signal transduction in the mitochondria, followed by activation of caspases and DNA fragmentation. The studies on detailed mechanism underlying the induction of apoptosis by N-Me (R) salsolinol are now in progress. (-) De-prenyl is an irreversible inhibitor of type B monoamine oxidase and now clin. used for an adjuvant for L-DOPA therapy. Considerable no. of in vivo and in vitro expts. demonstrate that (-) de-prenyl has neuroprotective or neuro-rescue effect. However, the mechanism of the neuroprotection has never been fully elucidated. The authors found that

not only (-) de-prenyl but also other propargylamines structurally related to (-) de-prenyl protected SH-SY5Y cells from apoptosis induced by N-Me (R) salsolinol. The study to clarify the mechanism of neuroprotection and the target mol. of propargylamines will lead to a way to develop new neuroprotective drugs for suppression or delay of the progression of Parkinson's disease.

L10 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2001 ACS
AN 1967:431137 CAPLUS
DN 67:31137
TI Comparative effects of streptonigrin derivatives on tissue culture cells
AU Mizuno, Nobuko S.
CS Univ. of Minnesota Med. Sch., Minneapolis, Minn., USA
SO Biochem. Pharmacol. (1967), 16(6), 933-40
CODEN: BCPCA6
DT Journal
LA English
AB In tissue culture cells, streptonigrin methyl ester (MES) was 1% as active as streptonigrin. MES inhibited the uptake of labeled precursors into RNA and DNA. Although its mode of action could not be distinguished from that of streptonigrin, this effect could not be accounted for by the liberation of free streptonigrin during metabolism. With isopropylidine azastreptonigrin (IPAS), no evidence could be found of cytotoxicity or biochem. effects on nucleic acids in concns. up to 10-3M. The degree of binding of IPAS to cells was 1/70 that with MES. IPAS had no effect on DNA synthesis even when the cell membrane barrier had been disrupted; therefore lack of cell penetration could not be invoked as an explanation for its inactivity. Since bridging the aminoquinone function of streptonigrin resulted in loss of biol. activity, it is suggested that the o-aminoquinone moiety may be important for the pharmacol. action of streptonigrin. 15 references.

L10 ANSWER 3 OF 3 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 1999386163 EMBASE
TI Involvement of an active efflux system in the natural resistance of Pseudomonas aeruginosa to aminoglycosides.
AU Aires J.R.; Kohler T.; Nikaido H.; Plesiat P.
CS P. Plesiat, Laboratoire de Bacteriologie, Hopital Jean Minjoz, 25030 Besancon Cedex, France. patrick.plesiat@ufc-chu.univ-fcomte.fr
SO Antimicrobial Agents and Chemotherapy, (1999) 43/11 (2624-2628).
Refs: 34
ISSN: 0066-4804 CODEN: AMACCQ
CY United States
DT Journal; Article
FS 004 Microbiology
030 Pharmacology

LA English
SL English
AB A mutant, named 11B, hypersusceptible to aminoglycosides, tetracycline, and erythromycin was isolated after Tn501 insertion mutagenesis of Pseudomonas aeruginosa PAO1. Cloning and sequencing experiments showed that 11B was deficient in an, at that time, unknown active efflux system that contains homologs of MexAB. This locus also contained a putative regulatory gene, mexZ, transcribed divergently from the efflux operon. Introduction of a recombinant plasmid that carries the genes of the efflux system restored the resistance of 11B to parental levels, whereas overexpression of these genes strongly increased the MICs of substrate antibiotics for the PAO1 host. Antibiotic accumulation studies confirmed that this new system is an energy- dependent active efflux system that pumps out aminoglycosides. Furthermore, this system appeared to function with an outer membrane protein, OprM. While the present paper was being written and reviewed, genes with a sequence identical to our pump genes, mexXY of P. aeruginosa, have been reported to increase resistance to erythromycin, fluoroquinolones, and organic cations in Escherichia coli hosts, although efflux of aminoglycosides was not examined (Mine et al., Antimicrob. Agents Chemother. 43:415-417, 1999). Our study thus shows that the MexXY system plays an important role in the intrinsic resistance of P. aeruginosa to aminoglycosides. Although overexpression of MexXY increased the level of resistance to fluoroquinolones, disruption of the mexXY operon in P. aeruginosa had no detectable effect on susceptibility to these agents.

ANSWER 6 OF 9 CAPLUS COPYRIGHT 2001 ACS
AN 1998:352961 CAPLUS
DN 129:37202
TI Novel polymeric complexes for the transfection of nucleic acids, with residues causing the destabilization of cell membranes
IN Midoux, Patrick; Monsigny, Michel
PA I.D.M. Immuno-Designed Molecules, Fr.; Midoux, Patrick; Monsigny, Michel
SO PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9822610	A1	19980528	WO 1997-FR2022	19971110

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,

GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

FR 2755976 A1 19980522 FR 1996-13990 19961115

FR 2755976 B1 19990115

AU 9851239 A1 19980610 AU 1998-51239 19971110

EP 946744 A1 19991006 EP 1997-945903 19971110

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

JP 2001504344 T2 20010403 JP 1998-523257 19971110

PRAI FR 1996-13990 A 19961115

WO 1997-FR2022 W 19971110

OS MARPAT 129:37202

AB The invention concerns a complex between at least a (neg. charged) nucleic acid and at least a pos. charged polymeric conjugate, the bond between the nucleic acid and the polymeric conjugate being electrostatic in nature, the polymeric conjugate contg. a polymer formed by monomer units bearing free NH3+ functions, and being such that: the free NH3+ functions of said monomer units are substituted in a ratio of .gtoreq.10 % by residues causing in weak acid medium destabilization of cell membranes, in particular the endocytosis vesicle membrane, and/or endosomes; said residues having further the following properties: they comprise a functional group for being fixed to said polymer, they are not active as recognition signal identified by a cell membrane receptor, they can comprise at least one free NH3+ function; said uncharged residues having further the following properties: they comprise at least a hydroxyl group, they are not active as recognition signal identified by a cell membrane receptor, the hydroxyl groups of said uncharged residues being capable of being substituted by at least a mol. which constitutes a recognition signal identified by a cell membrane receptor, with reservation that the whole set of free NH3+ functions is at least 30 % of the no. of monomer units of the polymeric network of said polymeric conjugate.

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USPT	l9 with l1	41	L12
USPT	l9 wiht l1	0	L11
USPT	histidi$	17289	L10
USPT	histidi$	17289	L9
USPT	histindi$	11	L8
USPT	l6 and l3	18	L7
USPT	l1 and l2	92	L6
USPT	l1 same l2	2	L5
USPT	l1 with l2	0	L4
USPT	polylysine	3250	L3
USPT	endosome or lysosome or membrane disrup$	2175	L2
USPT	quinol$	30185	L1